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Patent

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: BUECHLER et al.

Title: NOVEL METHODS FOR THE ASSAY OF TROPONIN I AND T AND COMPLEXES OF TROPONIN I AND T AND SELECTION OF ANTIBODIES FOR USE IN IMMUNOASSAYS

Appl. No.: 09/349,194

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Examiner: Gail Gabel

Art Unit: 1641

CERTIFICATE OF MAILING
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on the date below.

Line Gauthier
(Printed Name)

Line Gauthier
(Signature)

December 13, 2002
(Date of Deposit)

DECLARATION OF KENNETH F. BUECHLER

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

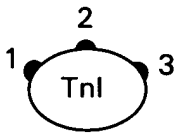
I, Kenneth F. Buechler, declare that:

1. I earned a Ph.D. in 1981 from the Department of Biochemistry, Indiana University . I have been engaged in research involving diagnostic assays for 17 years. A copy of my curriculum vitae is attached hereto as Appendix A. I am currently employed as Vice President, Research and Development, at BIOSITE, Inc., 11030 Roselle Street, San Diego, CA 92121. I am an inventor in the above-captioned patent application.

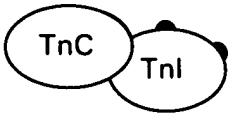
2. I have reviewed the above-captioned patent application, and the most recent office action received in the patent application.

3. It is my opinion that the skilled artisan could perform the methods as presently claimed using only methods that are both routine and well known in the art. In particular, methods for identifying antibodies that specifically bind to both free and complexed cardiac specific isoforms of troponin or, conversely, antibodies that distinguish between free and complexed cardiac specific isoforms of troponin, are described in detail in the present specification, and can be performed using only methods that are both well known and routine in the art.

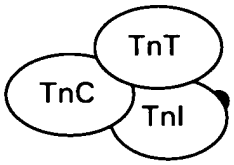
4. Taking cardiac specific troponin I ("TnI") as an example, the following drawings describes why it is possible for the skilled artisan to identify such antibodies. Troponin I contains certain antigenic sites that are "cardiac specific," meaning they are not present in non-cardiac forms of troponin I (for example, troponin I from skeletal muscle). These regions may be present as shown in red in this schematic drawing:



5. Binding of troponin C ("TnC") may obscure one or more of these cardiac specific regions so that it is not accessible to antibodies; however, one or more other cardiac specific regions may remain accessible. Antibodies may thus be selected that are specific for the free form of TnI (e.g., directed to site 1), or that bind both the free and binary complexed forms of TnI (e.g., directed to site 2 or 3):



6. Similarly, troponin T ("TnT") may also obscure one or more of these cardiac specific regions so that it is not accessible to antibodies; however, one or more other cardiac specific regions may remain accessible. Antibodies may thus be selected that bind the free and binary and ternary complexed forms of TnI (e.g., directed to site 3):



7. Thus, an assay system may utilize an antibody formed by pooling multiple antibody types in a cocktail, some of which recognize troponin only in complexes, some of which recognize only free troponin; alternatively, an assay system may utilize an antibody formed of one antibody type that recognizes a site that is available in both free and complexed troponin. This point is made clearly in the present application. For example, on page 24, lines 21-29, the specification states that "[t]he immunoassay can be formulated with a cocktail of antibodies to bind all the troponin complexes and the free troponin I and T. Alternatively, the immunoassay can be formulated with specific antibodies that recognize epitopes of the troponin I and T in the complexes and also the unbound troponin I and T."

8. The specification continues by providing examples of just such antibodies. For example, in Example 10, on page 63, lines 20-26, the specification notes that exemplary assays can be formulated to identify both free troponin I and binary troponin I complex, or that recognize only the free form. Similarly, in Example 15, on page 72, lines 12-27, the specification notes that

exemplary assays can be formulated to identify both free troponin I and ternary troponin I complex, or that recognize only the free form, or that recognize only the ternary complex.

9. It should be noted that the phrase "an antibody" recited in the claims would not be understood by the skilled artisan to imply a single molecule of antibody, but rather to refer to the population of antibody used in the particular assay.

10. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under § 1001 of Capital Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Sept 11, 2002
Date

Kenneth F. Buechler
Dr. Kenneth F. Buechler

#24 NW

CURRICULUM VITAE
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M. Sc., Biochemistry, Indiana University School of Medicine, Indianapolis, IN	Sept. 1976 – Oct. 1978
Research Associate, Indiana University School of Medicine, Indianapolis, IN	Oct. 1978 – Feb. 1979
Ph.D. Biochemistry, Indiana University School of Medicine, Indianapolis, IN	Mar. 1979 – June 1981
Predoctoral Research Fellow, Laboratory of Veterinary Biochemistry, State University Of Utrecht, Utrecht, The Netherlands	July 1980 – Dec. 1980
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KENNETH F. BUECHLER

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KENNETH F. BUECHLER

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